Applicants respectfully request reconsideration of the above-identified patent application as amended in view of the following remarks. No new subject matter has been added to the claims. The amendments to the claims are fully supported by the specification as originally filed. The amendments are made to clarify the claims, and are not intended to limit the scope of equivalents to which any claim element may be entitled.

Objection to the Specification

The Examiner has objected to the specification because in the specification the figures should be referred to in a manner consistent with how the Figures themselves are labeled. The Examiner has requested that appropriate correction is required for Figures 1A and 1B and Figures 3A and 3B. The specification has been amended as requested.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-30, 35 and 36

Claims 1-30, 35 and 36 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. It appears that the Examiner believes that the claims are enabled only for a polynucleotide with the sequence of SEQ ID NO:1, or a protein encoded by SEQ ID NO:2 and where the host cell is *S. cerevisiae*. Applicant respectfully traverses this rejection insofar as it relates to the pending claims.

Claim 1 is directed to a polynucleotide comprising a sequence encoding a functional vesicular fusion factor 2 protein (Vff2p), or a structural homolog of Vff2p. Independent claims 13 and 24 are directed to a polynucleotide expression vector or host cells encoding Vff2p, and independent claim 35 is directed to a Vff2p protein.

It is well-settled that it is not necessary that a patent applicant prepare and test all the embodiments of the invention in order to meet the requirements of 35 U.S.C. § 112. *Univ. of Calif. v. Eli Lilly*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997); *In re Angstadt* , 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Enablement is not precluded by the necessity for some

experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) "The key word is 'undue,' not 'experimentation.'" (emphasis in original). *Id.* The test is not merely quantitative, since a considerable amount of experimentation is in fact permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Id.* Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the *Wands* court, which cited the Board in *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Bd. Pat. App. & Int. 1986). The factors include the following: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

First, it should be noted that the Examiner admits that the relative skill of those in the art of recombinant engineering and protein expression in yeast is high (*Wands* factor 6). Second, even though the skill of art is high, the Examiner did not cite any prior art references against the present application. Therefore, clearly the Vff2p protein (and the corresponding nucleotide sequence, expression vectors, host cells and uses of these compositions) was a novel discovery by the present inventors in view of the state of the prior art (*Wands* factor 5).

The Examiner has stated that the area of the invention is unpredictable. The Examiner states that while some cellular components of the secretory and membrane fusion apparatus are able to function in a heterologous system, this is no indication that this will also be true for Vff2p. The Examiner's rejection is unclear to the Applicant. Is the Examiner stating that it is unpredictable for a homolog of Vff2p encoded by a sequence other than SEQ ID NO:1 (or amino acid sequence SEQ ID NO:2) to have the same function as that encoded by SEQ ID NO:1 (or amino acid sequence SEQ ID NO:2)? Or is the Examiner stating that it is unpredictable for there to be homologous Vff2p proteins in species besides *S. cerevisiae*? Or is the Examiner stating that it would unpredictable how a Vff2p from one species would function if placed in a host cell from a different species? Applicant would appreciate further clarification of the rejection.

Claims 31-34

Claims 31-34 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As discussed above, the Examiner admits that Vff2p is novel, and that the level of skill in the art is high. The Examiner argues, however, that there is no evidence that the present method of using Vff2p increases protein production in or protein secretion from the host cell.

Example 3D describes the observation that the overexpression of *VFF2* is correlated with an increased growth phenotype. In order for a cell to grow rapidly, it must produce and secrete any necessary plasma membrane and cell wall components at a high rate. *See*, specification at page 26, lines 12-18. Any protein that contains a signal peptide that targets it to be secreted outside the cell is also secreted at a high rate. Thus, a cell that is growing and dividing at a high rate must necessarily be producing and secreting proteins at a high rate.

The Examiner also states that the area of the invention is unpredictable, and that the claims could not be predictably carried out in the full scope based on knowledge in the prior art. As discussed in detail above, the Examiner admits that the relative skill and knowledge level of those in the art of recombinant engineering and protein expression is high. It is well within the level of skill of the art worker, in conjunction with the disclosure of the present application, to use Vff2p to increase protein production in or protein secretion from the host cell. Again, many yeast and non-yeast sequences have been introduced into and expressed by yeast cells and other types of host cells.

It is respectfully submitted that the pending claims 31-34 conform with 35 U.S.C. §112, first paragraph. Therefore, Applicant respectfully requests that the Examiner withdraw this 35 U.S.C. §112, first paragraph rejection.

Claims 37-42

No enablement rejections were raised regarding claims 37-42.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 6-11, 12, 17-22, 32, 34 and 36-42 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claims 6, 7, 11, 17, 18 and 22 are indefinite for the recitation of "first promoter" as there is no mention of another promoter in the claims. First, Application believes that the Examiner is actually means to refer to claims 6, 7, 17, and 18, as there is no mention of promoters in claims 11 and 22. Applicant has used the term "first promoter" in these claims so as to have proper antecedent basis for the term "second promoter" in the subsequent dependent claims 9 and 10, and 20 and 21.

The Examiner stated that claims 8-10, 19-21 and 42 are indefinite for the recitation of the term "target protein." In particular, the Examiner questions whether a "target protein" is Vff2p. The term "target protein, " "target heterologous protein" and "heterologous protein are used frequently throughout the specification. It is quite clear from the figure legend for Figures 1A and 1B at page 6 of the specification that the "target protein" is a protein other than Vff2p.

The Examiner states that there is not proper antecedent basis for the term "the target protein" in claims 9, 10, 20 and 21. Claims 9 and 10 directly or indirectly depend from claim 8, which recites "a target protein." Claim 9 has been amended to clarify that the second promoter is linked to the sequence recited in claim 8. Claims 20 and 21 directly or indirectly depend from claim 19. The term "a target protein" is properly set forth in claim 19 so as to provide antecedent basis for "the target protein" in claims 20 and 21.

The Examiner states that there is insufficient antecedent basis for the term "yeast" in claim 12. Claim 12 has been amended to recite "a yeast protein from" one of the recited organisms.

The Examiner stated that the term "essentially corresponding" is unclear in claim 36. The claim has been amended to recite "comprising."

The Examiner has stated that claims 31 and 33 are incomplete for omitting a step of culturing the cell. The claims have been amended to include this step.

The Examiner has stated that claims 37- 42 were rejected as being incomplete for omitting several steps, and that such omission amounts to a gap between the steps. In particular, the Examiner indicates that a step for constructing the recombinant cell and a step for inducing mutagenesis are essential steps that must be included prior to the step of growing the recombinant cell. Applicant traverses this rejection. It should be noted that the present claims are directed toward a method of selecting (growing the yeast a high temperature) a mutant cell. It is not important how the mutagenesis was induced in the starting material (which is clearly recited as being a yeast secretory mutant cell containing a polynucleotide sequence encoding a Vff2p, or a structural homolog of Vff2p operably linked to a first promoter).

The Examiner stated that claims 32 and 34 do not properly recite "the host cell." Claims 31 and 33 have been amended to provide proper antecedent basis for this term in claims 32 and 34.

The Examiner stated that claims 37-42 do not properly recite the term "the recombinant cell." Claim 37 has been amended to consistently recite "the secretory mutant cell."

Applicant respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

CONCLUSION

Applicants believe the claims are in condition for allowance and request reconsideration of the application and allowance of the claims. The Examiner is invited to telephone the below-signed attorney at 612-373-6961 to discuss any questions which may remain with respect to the present application. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date 11 September 2000 By _____
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner of Patents, Washington, D.C. 20231 on **September 11, 2000.**

Ann S. Viksnins
Name

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Signature